REMARKS

Claims 8, 10-13, 15, 16, 18-20, 29, and 30 are under examination in the present case. Each of these claims is rejected under 35 U.S.C. § 112, first paragraph. Claims 12, 15, 16, 18-20, 29, and 30 are further rejected under 35 U.S.C. § 112, second paragraph. The rejections are addressed below.

Support for the amendments

Support for the claim amendments is found throughout the specification. Support Support for the amendment of claim 15, which now recites "compared to AGE-1 gene expression in a nematode cell that is not contacted with said candidate compound," is found, for example, at page 31, lines 17-19. Support for the amendment of claim 16, which now recites "compared to AGE-1 PI 3-kinase activity in a cell in the absence of said candidate compound," is found, for example, at page 32, lines 9-11.

Applicants reserve the right to pursue all canceled subject matter in this, or future, related applications.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 8, 10-13, 15, 16, 18-20, 29, and 30 are rejected, under 35 U.S.C. § 112, first paragraph, based on the assertion that the claims fail to enable the skilled artisan to make and use the invention commensurate in scope with the claims. While applicants disagree with this assertion, in order to expedite prosecution, and in view of the Office's suggestions, amended claim 8 now recites "an AGE-1 polypeptide, said polypeptide

having the sequence of SEQ ID NO: 1." This basis for the rejection of independent claim 8, and claims 10-13, 16, 19, and 20, which recite the DNA of claim 8 should be withdrawn.

Claims 15 and 18-20 are further rejected, under 35 U.S.C. § 112, first paragraph, as also lacking enablement on other grounds. This enablement rejection turns on the following assertions: (i) that the specification fails to teach how to determine that the transcription of the *age-1* gene has been altered; (ii) that the specification fails to teach the appropriate controls for determining that the transcription of the *age-1* gene has been altered; and (iii) that the specification fails to teach methods for the selection of a compound for use in the instant invention. . This rejection is respectfully traversed.

Contrary to the Office's assertions, applicants have provided a teaching in the present specification that enables the skilled artisan to practice the methods of the invention. With respect to detecting a change in the transcription of *age-1*, applicants disclose, at page 31, lines 15-17, that *age-1* expression may be measured, for example, by standard Northern blot analysis using an *age-1* nucleic acid, or fragment thereof, as a hybridization probe. Applicants teach the nucleic acid sequence of an *age-1* cDNA at Figure 4 (SEQ ID NO:2) and disclose, at page 31, lines 15 and 16, that Ausubel et al. (*Current Protocols in Molecular Biology*, 1996, Wiley & Sons, New York, NY) provide methods for carrying out a Northern blot.

With respect to teaching the appropriate controls, applicants disclose, at page 31, lines 9-14, that *age-1* expression may be measured following the addition of antagonist molecules either to culture medium or to an animal, for example, a nematode. Applicants

further disclose, at page 31, lines 17-19, that the level of *age-1* expression in the presence of a candidate molecule is compared to the level measured for the same cells in the absence of the candidate molecule.

With respect to the selection of candidate compounds, applicants teach, at page 31, lines 19-21, that preferred candidate modulators are those that decrease AGE-1 expression. At page 32, lines 1-7, applicants also teach that such compounds may be purified from a mixture using HPLC or FPLC until a single compound is demonstrated to modulate AGE-1 expression. Applicants further disclose, at page 33, lines 4 and 5, that the usefulness of compounds, found to effectively modulate AGE-1 expression, can be confirmed by testing the compounds in animal models, for example, in nematodes. Finally, applicants disclose, at page 33, lines 6-9, that selected compounds may be used as therapeutics to decrease the level of native *age-1* expression and thereby increase the longevity of an animal, for example, a human.

In view of these teachings in the specification, it is clear that applicants have provided an enabling description that would instruct the skilled artisan how to measure *age-1* expression, how to employ the appropriate controls, and how to select compounds that alter *age-1* expression. These bases for the enablement rejection should also be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 12, 15, 16, 18-20, and 29-30 are further rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. As applied to the current claims, this rejection is respectfully traversed.

The rejection of independent claims 15 and 16, and their dependent claims 19 and 20, has been overcome by the amendment of claims 15 and 16.

The rejection of claim 12 appears to be in error. This rejection was not explained in the Office action, nor does the rejected language of claims 15 or 16 appear in claim 12. Applicants request clarification on this point.

Claims 18, 29, and 30 have been canceled, and the rejection as applied to these claims is moot.

CONCLUSION

Applicants submit that this case is in condition for allowance, and such action is respectfully requested. If the Office does not concur, a telephonic interview with the undersigned is hereby requested.

A marked-up version indicating the amendments to the claims, as required by 37 C.F.R. § 1.121 (c)(1)(ii), is enclosed.

A clean version of all pending claims is also enclosed.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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Version of Claims Showing Changes Made, Pursuant to 37 C.F.R. § 1.121(c)(1)(ii)

8. (Thrice Amended) A purified and isolated DNA which encodes an AGE-1 polypeptide, [having PI 3-kinase activity,] said polypeptide [having at least 95% amino acid sequence identity to] comprising the sequence of [the full length polypeptide of Figure 6 (] SEQ ID NO: 1 [) and comprising a p85-binding domain and a lipid kinase domain.]

15. (Thrice Amended) A method of identifying an AGE-1 modulatory compound that is capable of decreasing the expression of an AGE-1 gene, said method comprising the steps of:

(a) providing a nematode cell expressing [the] its endogenous AGE-1 DNA [of claim 8],

(b) contacting said nematode cell with a candidate compound; and

(c) measuring AGE-1 gene expression in said nematode cell, a decrease in AGE-1 gene expression in said nematode cell following contact with said candidate compound, [relative] compared to AGE-1 gene expression in [an untreated] a nematode cell that is not contacted with said candidate compound, identifying said candidate compound as a compound that is capable of decreasing AGE-1 gene expression.

16. (Four Times Amended) A method of identifying an AGE-1 modulatory compound that is capable of decreasing AGE-1 PI 3-kinase activity, said method comprising the steps of:

(a) providing a cell expressing an AGE-1 polypeptide of claim 8;

(b) contacting the cell with a candidate compound; and

(c) measuring the PI 3-kinase activity of said cell, a decrease in AGE-1 PI 3-kinase activity of said cell following contact with the candidate compound, [relative] compared to AGE-1 PI 3-kinase activity in [an untreated] a cell that is not contacted with said candidate compound, identifying said candidate compound as a compound that is capable of decreasing AGE-1 PI 3-kinase activity.

Clean Version of All Pending Claims

8. (Thrice Amended) A purified and isolated DNA which encodes an AGE-1 polypeptide, said polypeptide comprising the sequence of SEQ ID NO: 1.

10. (Amended) A vector comprising the purified and isolated AGE-1 DNA of claim 8.

11. (Amended) A cell comprising the purified and isolated AGE-1 DNA of claim 8.

12. (Twice Amended) A method of producing a recombinant AGE-1 polypeptide, said method comprising the steps of:

(a) providing a cell transformed with the DNA of claim 8 encoding an AGE-1 polypeptide, said DNA being expressed in the cell;

(b) culturing the transformed cell under conditions for expressing the DNA; and

(c) isolating the recombinant AGE-1 polypeptide.

13. A recombinant AGE-1 polypeptide produced according to the method of claim 12.

15. (Thrice Amended) A method of identifying an AGE-1 modulatory compound that is capable of decreasing the expression of an AGE-1 gene, said method comprising the steps of:

(a) providing a nematode cell expressing its endogenous AGE-1 DNA,

(b) contacting said nematode cell with a candidate compound; and

(c) measuring AGE-1 gene expression in said nematode cell, a decrease in AGE-1 gene expression in said nematode cell following contact with said candidate compound, compared to AGE-1 gene expression in a nematode cell that is not contacted with said candidate compound, identifying said candidate compound as a compound that is capable of decreasing AGE-1 gene expression.

16. (Four Times Amended) A method of identifying an AGE-1 modulatory compound that is capable of decreasing AGE-1 PI 3-kinase activity, said method comprising the steps of:

(a) providing a cell expressing an AGE-1 polypeptide of claim 8;

(b) contacting the cell with a candidate compound; and

(c) measuring the PI 3-kinase activity of said cell, a decrease in AGE-1 PI 3-kinase activity of said cell following contact with the candidate compound, compared to AGE-1 PI 3-kinase activity in a cell that is not contacted with said candidate compound, identifying said candidate compound as a compound that is capable of decreasing AGE-1 PI 3-kinase activity.

19. (Amended) The method of claim 15 or 16, wherein said method is carried out in a nematode

20. The method of claim 15 or 16, wherein said method involves assaying AGE-1 PI 3-kinase activity *in vitro*.